R E M A R K S

Claim Amendments

Claim 6 was amended to include the feature of claim 7.

Claims 7, 9 and 11 were canceled.

Claim 12 was amended to include the feature of claim 13.

Claims 13, 15 and 17 were canceled.

Rule 116

Entry of the above claim amendments is respectfully requested, since the amendments involve features that were set forth in the claims prior to the final rejection.

Presently Claimed Invention

Applicants' claim 6 relates to an aqueous ophthalmic solution comprising 0.005% (W/V) latanoprost as an active ingredient, wherein the latanoprost is stabilized to be stored at room temperature by adding ε-aminocaproic acid to the solution.

Applicants' claim 12 pertains to an aqueous ophthalmic solution comprising 0.005% (W/V) latanoprost as an active ingredient, wherein the latanoprost is stabilized to be stored at

room temperature by adjusting the pH of the solution to 5.0 to 6.25 and adding ε-aminocaproic acid to the solution.

In summary, applicants' present claims are directed to an aqueous ophthalmic solution comprising 0.005% (W/V) latanoprost as an active ingredient, wherein the latanoprost is stabilized to be stored at room temperature by (i) adding ε-aminocaproic acid to the solution or (ii) by adjusting the pH of the solution to 5 to 6.25 and adding ε-aminocaproic acid to the solution.

Obviousness Rejection under 35 USC 103

Claims 6 to 17 were rejected under 35 USC 103 as being unpatentable over USP 6,011,062 to Schneider et al. and further in view of USP 5,556,848 to Kimura et al. for the reasons indicated on pages 2 to 3 of the February 20, 2009 Office Action.

It was admitted in the previous Office Action of June 3, 2008 that Schneider et al. differ from the instant claims insofar as Schneider et al. do not teach adding ε-aminocaproic acid to an ophthalmic solution.

It was further admitted in the previous Office Action of June 3, 2008 that Kimura et al. do not teach the use of latanoprost.

Kimura et al. (USP 5,556,848) disclose an ophthalmic suspension comprising difluprednate. Kimura et al. also disclose that a water soluble polymer is added for enhancing dispersion stability in the ophthalmic suspension containing water-insoluble difluprednate (column 2, lines 27 to 37). Kimura et al. disclose that nonionic surfactants, such as polyoxyethylene hydrogenated castor oils can be added in their suspension for enhancing the dispersion stability (column 3, lines 34 to 49). Moreover, Kimura et al. disclose in column 3, lines 19 to 33 that acetates and ε-aminocaproic acid are useful as buffers to suppress formulation of agglomerates, prevent lowering of pH, and provide a suspension superior in redispersibility and stability.

As discussed above, Kimura et al. teach enhancing the dispersion stability in an ophthalmic suspension containing water-insoluble difluprednate (physical stabilization). In contrast thereto, applicants' present claims 6, 8 and 10 relate to enhancing the chemical stability of latanoprost dissolved in water (chemical stabilization). Stated differently, since the problem sought to be resolved in Kimura et al. was to stabilize the dispersion of the suspended ophthalmic solution, whereas the presently claimed invention seeks to chemically stabilize the

active ingredient (latanoprost) in a water-soluble ophthalmic solution, Kimura et al. and the presently claimed invention substantially differ from each other in what is stabilized.

Further, since the active principle of Kimura et al. is difluprednate, whereas the active ingredient of the presently claimed invention is latanoprost, Kimura et al. and the presently claimed invention completely differ from each other also in the chemical structure and the chemical properties of the respective active ingredient. This difference is acknowledged at the bottom of page 2 of the February 20, 2009 Office Action.

Furthermore, although Kimura et al. disclose that ε-aminocaproic acid enhances the dispersion stability of their suspended ophthalmic solution, there is no teaching or suggestion in Kimura et al. of the chemical stability of the active ingredient in a water-soluble ophthalmic solution.

Schneider et al. teach storage-stable prostaglandin compositions and disclose that the use of polyethoxylated castor oils in the compositions enhances the chemical stability of the prostaglandins in the compositions (column 1, lines 52 to 56). Further, Figs. 1 and 2 of Schneider et al. show that the addition of polyethoxylated castor oils (Cremophor® EL and Alkamuls®

EL-620) increases the chemical stability of prostaglandin (Compound No. 2) as compared with the case where a surfactant (Polysorbate 80) is added.

However, the polyethoxylated castor oil used in Schneider et al. is a polymer classified as PEG-5 to PEG-200 hydrogenated castor oils, whereas ε-aminocaproic acid used in the presently claimed invention is a low-molecular compound represented by following formula: $H_2NCH_2CH_2CH_2CH_2COOH$. Polyethoxylated castor oil used in Schneider et al. and ε-aminocaproic acid recited in applicants' claims completely differ from each other in their chemical structure and their chemical properties. This difference was acknowledged at the bottom of page 2 of the February 20, 2009 Office Action.

The present specification on pages 12 to 15 describes, in stability tests of latanoprost, the residual ratio of latanoprost after storage at a temperature range of 50°C to 80°C for the period of 4 to 8 weeks. Applicants have informed the undersigned that in the field of ophthalmic solutions, the storage-stability of a drug at room temperature over along period is generally presumed from an accelerated test conducted at a high

temperature. Therefore, applicants' present claims are consistent with the disclosure of the present specification.

In view of the above, it is respectfully submitted that one of ordinary skill in the art would not arrive at the presently claimed invention (i.e., adding ε-aminocaproic acid to enhance the chemical stability of latanoprost) based on the disclosures of Schneider et al. and Kimura et al.

It is therefore respectfully submitted that applicants' claims 6, 8 and 10 patentably distinguish over the references, singly or combined.

Applicants' claims 12, 14 and 16 relate to a further enhancement of the chemical stability of latanoprost by adding ε-aminocaproic acid within a specified pH range of 5.0 to 6.25. As discussed in the preceding paragraph, applicants' claims 6, 8 and 10 are considered to be patentable over the references. Therefore, applicants' claims 12, 14 and 16, characterized by specifying a pH range of 5.0 to 6.25, are also considered to be patentable over the references, singly or combined.

Table 3 on page 16 of the present specification (which is reproduced hereinbelow) shows that after storage at 50°C for 8 weeks, the residual ratio of the latanoprost in an ophthalmic

solution is 93.1% when ε-aminocaproic acid is added to the solution. Moreover, Table 3 shows that after storage at 80°C for 4 weeks, the residual ratio of latanoprost is 51.8% when ε-aminocaproic acid is added, whereas the residual ratio of latanoprost is 6.3 to 28.9% when ε-aminocaproic acid is not added. Thus, applicants' Table 3 clearly shows that the stability of latanoprost in an aqueous ophthalmic solution is significantly improved when ε-aminocaproic acid, out of numerous additives, is added. This increased stability afforded by the presently claimed invention was acknowledged at the bottom of page 3 of the February 20, 2009 Office Action.

Table 3

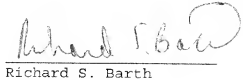
	Additives	Storage at 50°C for eight weeks	Storage at 80°C for four weeks
Formulation 1	Crystalline sodium dihydrogenphosphate	88.7%	24.0%
Formulation 2	PEG 400	88.8%	25.9%
Formulation 3	Propylene glycol	88.1%	26.1%
Formulation 4	Trehalose	83.7%	26.4%
Formulation 5	Isopropanol	88.9%	28.9%
Formulation 6	α-Cyclodextrin	86.6%	22.1%
Formulation 7	Citric acid	87.1%	6.3%
Formulation 8 according to the presently claimed invention	ε-Aminocaproic acid	93.1%	51.8%

Withdrawal of the 35 USC 103 rejection is therefore respectfully requested.

Reconsideration is requested. Allowance is solicited.

If the Examiner has any comments, questions, objections or recommendations, the Examiner is invited to telephone the undersigned at the telephone number given below for prompt action.

Respectfully submitted,



Frishauf, Holtz, Goodman
& Chick, P.C.
220 Fifth Ave., 16th Floor
New York, NY 10001-7708
Tel. No.: (212) 319-4900
Fax No.: (212) 319-5101
E-Mail Address: BARTH@FHGC-LAW.COM
RSB/ddf

Richard S. Barth
REG. NO. 28,180

Enclosure: PETITION FOR EXTENSION OF TIME